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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/617,545	07/14/2000	Toshio Ariyasu	Ariyasu=1A	5549

1444 7590 08/06/2002

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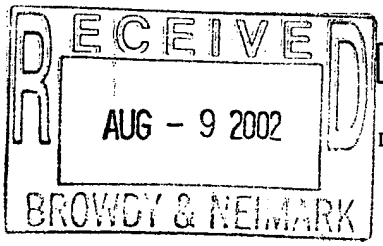

EXAMINER	
KAUFMAN, CLAIRE M	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/06/2002

~~11~~ 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Final=6NO2002
DKT 8.9.02

Office Action Summary	Application No. 09/617,545	Applicant(s) ARIYASU ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/9/02, 5/13/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,11-14 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,11-14 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The amendments filed 5/9/02 and 5/13/02 have been entered.

Response to Amendment

The rejections of claim 1 are moot in view of the cancellation of the claims

The rejection of claims 3 and 4 under 35 USC 112, first paragraph, is withdrawn in view of the amendments to the claims.

The rejection of claims 11 and 12 under 35 USC 112, second paragraph, is withdrawn in view of the amendment to the claims which introduce the omitted method step (claim 11) and clarify transformation (claim 12). Note that claim 11 remains rejected as set forth below.

The rejection of claim 5 under 35 USC 112, second paragraph, is withdrawn in view of the amendment to the claim.

The rejection of claims 2-5 under 35 USC 102(a) is withdrawn in view of the amendment to the claims.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The disclosure remains objected to because of the following informality: On page 4, fourth line in the paragraph beginning "In FIG. 1,", "*coli*;t he" should be ""*coli*; the".

Applicants' request that the Examiner correct the informality when the claims are allowable is acknowledged.

Claim Objections

Claims 18 and 19 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since the independent claims from which 18 and 19 depend require a specific nucleotide sequence (SEQ ID NO:5 or 6), these dependent claims cannot be degenerates thereof.

Note that claim 5 is not subject to this objection since SEQ ID NO:4 can and is contained within a larger coding sequence (SEQ ID NO:5) and, therefore, the claimed DNA can have degeneracy of the coding sequence outside SEQ ID NO:4.

Claim Rejections - 35 USC § 112, First Paragraph

Claims 2, 5-7 and 11-14 remain and new claim 17 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA comprising SEQ ID NO:5 or 6 or encodes a protein comprising the sequence of SEQ ID NO:2 or 3 (*i.e.*, a degenerate DNA), does not reasonably provide enablement for a DNA that is not one of the above but which must still encode a hedgehog or desert hedgehog protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the reasons set forth in the previous Office action (paper #8, pages 4-5), and for the following reasons addressing the new claims. Claim 17, while reciting some structural similarity (see rejection under 35 USC 112, second paragraph, below), has no reference sequences to which one can determine if the structurally similarity limitation is met. Regardless, for the reasons set forth in the previous Office action, the specification is not enabling for the DNA of claim 17.

Applicants state (#9, middle of page 6) that the rejection does not apply to all claims, but only to claims 2-4. The argument has been fully considered, but is not persuasive. As stated above, due to amendment of the claims, claims 3 and 4 are no longer rejected, but claims 2, 5-7 and 11-14 remain and new claim 17 are rejected. The independent claims rejected are claims 2 and 11, with the dependent claims not adding enabling limitations.

To reiterate, independent claim 11 has no structural or functional limitations. The term "desert hedgehog protein" has no limiting definition in the specification or prior art so that what precisely is encompassed by it in terms of structure or function is known. As set forth in the previous Office action in the last paragraph on page 5:

> There is no disclosure of a function of the claimed HuDhh. There is no guidance for making a DNA without knowing what it looks like or what it does. The specification does not provide limitations on what portion(s) of a DNA must be the same as SEQ ID NO:5 or what minimum shared sequence identity must be present for DNA to be considered an HuDhh-encoding polynucleotide. Note that the language "contains a part

or the whole of ...SEQ ID NO:5" (claim 3), does not provide a structural limitation since a part can be one nucleotide. Because the hh family has not only Dhh but also Shh and Ihh, which share sequence identity and have some shared functions like binding patched receptor, it is not straight forward to say that a protein is a Dhh if there is no structure to distinguish it from a Shh or Ihh protein and a function specific to Dhh and not the other proteins of the hh family....

In reference to claim 2 and dependent claims, Applicants argue in paper #10, page 4 of the response, that SEQ ID NO:4, which encodes SEQ ID NO:1, encodes a mature human Dhh, and not a fragment of the mature form, pointing to pages 24, 28 and 33 of the specification for support. The argument has been fully considered, but is not persuasive. It does appear that SEQ ID NO:4 encodes "a mature form" of human Dhh, however, the specification fails to provide the skilled artisan with guidance or examples of how to use the 176 amino acid long mature form. It is half the size of the other disclosed HuDhh mature form of SEQ ID NO: 2 and mouse Dhh, both of which are 374 amino acids long. Making a monoclonal antibody or hybridoma to produce the monoclonal antibody (*e.g.*, p. 46, last paragraph) is not an enabling use if one does not know how to use the protein to which the antibody binds.

New:

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17 is drawn to a DNA encoding a desert hedgehog protein of human origin at least 80% homology to DNAs from mouse Dhh, human or mouse Ihh, or mouse, chicken, human or zebrafish Shh which is not identical to said Shh proteins. The specification has taught a single human "desert" hedgehog protein having the full length sequence of SEQ ID NO:3, mature of SEQ ID NO:2 or 1, both of which are comprised within SEQ ID NO:3. No other human desert hedgehog protein of human origin is taught. Further, the 80% identity is not to any particular sequence but to a potential genus of proteins. It is not known if there are, for example, splice variants or polymorphisms of other hedgehog proteins to which the one(s) encoded by the claimed DNA have the necessary structural similarity.

The specification discloses SEQ ID NO:4-6, the sequences of nucleic acids encoding the human Dhh protein having the sequence of SEQ ID NO:1-3, respectively, all of which comprise SEQ ID NO:1. SEQ ID NO:4-6 meet the written description provision of 35 USC 112, first paragraph. However, the claims are directed to or encompass sequences that are 80% homology to other hedgehog proteins having no limiting structural features, which include sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a recited degree of identity, and so forth. None of these sequences meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO:4-6 or DNAs which encode SEQ ID NO:1-3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 11 and 14 remain and new claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11, 14 and 17 are indefinite because it is unclear what distinguishes a desert hedgehog (Dhh) protein from other proteins, particularly other hedgehog proteins. As a result, the metes and bounds of the claims is not clear.

Applicants argue (paper #9, page 5) that the claims are not confusing. This argument is not persuasive because neither the prior art nor instant specification provide a limiting definition such that the skilled artisan could tell when in possession of a Dhh described only by name in the absence of any other identifying features such as structure or function.

New:

Claims 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite because it recites "has a DNA identity of at least 80% homology to either of DNAs of ...." The claim raises 3 new issues under 35 USC 112, second paragraph.

The first problem comes from "identity of at least 80% homology". It is not clear what the difference between identity and homology is. The precise meaning of "homology" in biological terms is: having a common origin. Reeck et al. (1987, Cell, 50: 667) explain that it is "a concept of quality ... a type of relationship between two or more things. Thus, amino acid or nucleotide sequences are either homologous or they are not. They cannot exhibit a particular "level of homology" or "percent homology.""

The second problem comes from the use of the term "either" of DNAs A, B,.. and D, E,... and, G, H..., since either is used to refer to "this or that", not multiple possibilities which are not set forth in the alternative.

The third problem stems from the ambiguity of what is and what is not excluded. It appears that this claim does not exclude DNAs which encode Ihh of human origin. There is no

limiting definition of a "desert hedgehog protein" and there are no structural limitations of the proteins set forth in the claims.

Note, this claim is also indefinite for reasons set forth in the previous Office action as discussed above relating to metes and bounds of a Dhh protein.

Claims 18 and 19 are indefinite because in the last sentence the phrase "encoding amino acid sequence" is used. Because nucleotide sequences are the "encoding" sequence, the claim is confusing. Amino acid sequences are the "encoded" sequence. It is unclear if Applicants intended that the "encoding" or "encoded" amino acid sequence is conserved.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 17 is rejected under 35 U.S.C. 102(a) as being anticipated by Drummond et al. (GenBank Accession No. U59748, also known as BC, cited by Applicants).

Drummond (GenBank Accession No. U59748) teaches part of the nucleic acid encoding a human Dhh protein and the corresponding deduced amino acid sequence. The sequence isolated was mRNA, but that shown is DNA.

Note that the claimed has no minimum size or functional limitation.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**.. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.
Patent Examiner, Art Unit 1646
August 1, 2002

LORRAINE SPECTOR
PRIMARY EXAMINER